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SUSCEPTIBILITY OF RABBITS TO THE VIRUS OF MEASLES

INOCULATIONS WITH NASOPHARYNGEAL MATERIAL

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The investigation, the results of which are reported now, was undertaken to determine whether the inoculation of nasal secretions from patients with measles would produce definite and characteristic symptoms in rabbits; it was carried on at the same time, and with material from the same patients as were used by Nevin¹ in her work on blood inoculations.

The nasopharynx of patients in the early eruptive, or pre-eruption stage of measles was irrigated with 30-50 cc normal salt solution. Cultures were made from the material thus obtained, on blood-vitamine-agar to establish the prevalent types of bacteria. From 5-10 cc of the washings were injected into the trachea of rabbits, the animals being lightly anesthetized. In most animals this amount of fluid caused a leakage from the nose, showing that the mucous membrane of the upper air passage was thoroughly flooded with infectious material. Unfiltered washings were used in most cases, as it was believed that the usual flora of the upper respiratory tract would not cause characteristic symptoms in rabbits. Only a small number of rabbits received material passed through a Berkefeld V candle. Aerobic cultures from these filtrates were uniformly negative for the test organism (*B. prodigiosus*).

The majority of rabbits (table 1) gave a certain reaction, yet apparently there are among them a fairly large number of refractory individuals, for in a number of instances in this series, only one animal out of two inoculated with the same nasal washings developed symptoms, and even when both succumbed, there was often considerable difference in the severity of symptoms. In susceptible animals the incubation period varied between two and seven days.

The least reliable and constant symptom seems to be the enanthem; while present in about 20% of the cases, only 5 animals showed what

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¹ J. Infect. Dis., 1921, 29, p. 429.

TABLE 1
RABBIT INOCULATIONS WITH NASOPHARYNGEAL WASHINGS

Case	Rabbit No.	Exanthem						Desquamation			Coryza			Conjunctivitis			Enanthem		Temperature Extremes	Leukopenia			Remarks
		Erythematous			Maculopapular			In-tensity	Day of Onset	Duration	In-tensity	Day of Onset	Duration	In-tensity	Day of Onset	Duration	In-tensity	Day of Onset		Duration			
		In-tensity	Day of Onset	Duration	In-tensity	Day of Onset	Duration																
M19	191	++	2	2	2	9	102.2-102.8	Died after 4 days; dysentery
M20	192	+	2	2	12	3	102.6-102.8	+	10	1	
M21	201	3	3	101.3-103	+	2	1	
M22	211	++	2	2	2	2	1	6	1	102.1-105	++	3	1	Died after 4 days; bronchopneumonia
M23	221	+	2	4	4	4	2	2	1	100.8-102.4	+	3	2	Filtered material inoculated
M24	231	++	2	4	3	3	102.1-104.8	+	2	2	
M25	241	++	2	5	5	5	100.8-102	+	3	1	
M26	251	6	6	5	3	99.4-100.8	+	3	1	
M27	261	7	7	5	6	1	99.6-103.1	+	8	1	Phlegmon of abdominal wall
M28	282	10	10	3	6	101.8-104.7	+	7	1	
M29	291	++	2	2	7	1	101.7-105.4	+	4	1	
M30	292	++	2	2	11	11	5	3	102.1-105.8	++	5	1	Died of rabbit septicaemia
R1	301	+	2	2	12	12	4	6	101.8-107	+	2	2	Died after 4 days; bronchopneumonia
D1	311	+	2	2	14	14	5	4	101.4-101.3	Filtered material inoculated
D2	321	Died within 24 hours
S1	331	5	5	
S2	341	+	4	4	1	1	7	

* Scratches ?

TABLE 2
PASSAGE EXPERIMENTS AND INOCULATIONS WITH CULTIVATED VIRUS

Case	Rabbit No.	Exanthem						Desquamation			Coryza			Conjunctivitis			Enanthem		Temperature Extremes	Leukopenia			Remarks
		Erythematous			Maculopapular			In-tensity	Day of Onset	Dura-tion	In-tensity	Day of Onset	Dura-tion	In-tensity	Day of Onset	Dura-tion	In-tensity	Day of Onset					
		In-tensity	Day of Onset	Dura-tion	In-tensity	Day of Onset	Dura-tion													In-tensity	Day of Onset	Dura-tion	
M21	213	+	2	2	±	4	1	2	2	2	1	±?	2	102.2-102.4	+	3	1	Inoculated with filtered lung tissue from R 212			
	214	±	3	1	3	1	101.6-102.2	Inoculated with filtered blood culture R 212			
	215	101.6-102	Inoculated with nasal discharge from R 212			
	272	+	5	1	+	6	2	5	2	102.3-103.6	++	7	1	Inoculated with unfiltered lung tissue R 271; died 8th day			
M28	281	++	2	5	..	2	+	5	4	2	2	2	2	±	1	103 -103	Both inoculated with 2d transfer of a culture of filtered nasal washings, M 28			
	282	+	2	2	+	+	+	7	7	2	2	2	..	+	2	102 -102.4	Inoculated with blood from R 281-282 (pooled)			
M29	283	+	3	2	+	3	2	+	13	6	5	1	..	+	2	Inoculated with blood from R 281-282 (pooled)			
	284	3	4	..	+	3	Inoculated with blood from R 283			
	285	±	3	1	+	5	+	10	6	4	6	6	..	++	Both inoculated with blood culture from R 281, second transfer			
	286	+	3	4	+	10	5	3	4	4	..	+	Inoculated with culture from filtered nasal washings; patient M 29, second transfer			
M29	293	..	2	8	+	6	3	+	11	3	2	6	..	++	2	Inoculated with culture from filtered nasal washings; patient M 29, second transfer			
	294	++	+	9	5	2	2	4	..	+	2	102	Inoculated with culture from filtered nasal washings; patient M 29, second transfer			
	295	..	2	1	+	4	2	7	2	..	+	2	Inoculated with culture from filtered nasal washings; patient M 29, third transfer			
	296	+	+	3	2	2	1	+	Inoculated with culture from filtered nasal washings; M 29, fifth transfer			
	297	+	4	2	+	5	4	+	10	3	5	2	..	+	Inoculated with culture from filtered nasal washings; M 29, fifth transfer			

one might describe as good typical Koplik spots. The temperature curve also is not at all characteristic; in very few animals did the temperature go above 103. In some of the cases a certain relationship appeared between the temperature curve, the cutaneous symptoms and the leukocyte count; however, it was far from constant, and the fluctuations noted in daily blood counts made for one week before inoculation do not make a "leukopenia" seem a very dependable diagnostic sign in rabbits. In a number of animals a distinct polychromatophilia was noted.

Conjunctivitis and inflammation of the upper respiratory passages, in varying degrees of severity, occurred in 70% of animals; it is not always possible to eliminate "snuffles," but the appearance of coryza together with the rash, and its brief duration in most cases, point against its being an intercurrent infection. Seventy-five per cent. of the rabbits showed some form of cutaneous eruption, either a diffuse, punctate erythema, which in 3 severe (2 fatal) cases became petechial, or, sometimes following the erythema, sometimes occurring without it, a maculopapular rash, which faded after 2-4 days and left pigmentation persisting until desquamation began.

Desquamation, either branny or flaky, occurred in all but 4 animals after the rash and was noted 3 times in cases in which no rash had been noted (3 animals with marked erythema died before desquamation occurred).

Control animals were inoculated with nasopsaryngeal washings from 1 case of nasal catarrh, 2 cases of diphtheria and 2 of scarlet fever. There was desquamation in the 2 scarlet fever animals, preceded in one case by a rash which was, however, different in character from that shown by the measles rabbits. The other animal, showing 2 macules, presented other evidences of clawing and scratching over some of the unshaved portions of his skin.

Passage experiments from rabbit to rabbit were unsuccessful when nasal discharges were used, owing probably to the scantiness of material. Successful inoculations were made in 7 cases, using, 3 times, 2 cc of blood, and, twice, a suspension of lung tissue from severe and fatal cases. The other passage experiments were conducted with rabbit blood cultures. Attempts have also been made to cultivate a specific organism from the filtered nasal washings from patients, and while the work along these lines is incomplete, the reactions obtained in rabbits inoculated with the fifth transfer of such cultures indicated

at least that the virus remains alive and virulent at 37 C. for 24 days. The results obtained by reinoculating convalescent animals have thus far been rather contradictory, and frankly successful in only two cases.

It cannot be claimed that the results obtained in any one animal give a clear and typical picture of measles, yet taking the series as a whole, there has been enough conformity to encourage the belief that rabbits are susceptible to the virus of measles and within rather wide limits give a characteristic syndrome.

Note.—E. Harde, in the *Compt. Rend. Soc. de biol.*, 1921, 84, p. 968, makes a short communication on the transmission of measles from man to rabbit by means of intravenous inoculation with blood. She states that an erythema develops within 48 hours and lasts from 24 to 48 hours. The blood of a scarlet fever patient produced only a slight reddening after the same interval of time, but no real erythema. These injections were made at this laboratory a number of years ago, but the results were not considered conclusive enough to follow up or to publish, until Dr. Harde saw the rabbits described in the present articles.